CLAIMS

WHAT IS CLAIMED IS:

1. An isolated polynucleotide encoding a polypeptide having stem cell growth factor activity, said polynucleotide comprising the nucleotide sequence of SEQ ID NO: 9, 11, 12, 31 or 33 or the mature protein coding portion thereof, or a fragment, analog, variant or derivative thereof that encodes a polypeptide retaining stem cell growth factor activity.

2. The polynucleotide of claim 1 which hybridizes to the complement of the nucleotide sequence of SEQ ID NO: 9, 11, 12, 31 or 33 under stringent hybridization conditions.

3. The polynucleotide of claim 1 which comprises a nucleotide sequence having greater than about 85% sequence identity with the nucleotide sequence of SEQ ID NO:9, 11, 12, 31 or 33.

4. The polynucleotide of claim 1 which comprises a nucleotide sequence having greater than about 90% sequence identity with the nucleotide sequence of SEQ ID NO:9, 11, 12, 31 or 33.

5. The polynucleotide of claim 3 comprising a nucleotide sequence having greater than about 92% sequence identity with the nucleotide sequence of SEQ ID NO:9, 11, 12, 31 or 33.

6. The polynucleotide sequence of any of claims 1, 2 or 3 with the proviso that said polynucleotide sequence does not consist of the nucleotide sequence of SEQ ID NO: 47.

7. An isolated polynucleotide that comprises the mature protein coding sequence of SEQ ID NO: 9. 11, 12, 31 or 33.

8. An isolated polynucleotide that comprises the nucleotide sequence of SEQ ID NO: 9, 11, 12, 31 or 33.

9. The DNA of claim 1 encoding:

(A) a polypeptide which has an amino acid sequence comprising at least amino acid residues 22 to 279 of SEQ ID NO: 32, or an amino acid sequence comprising at least amino acid residues 22 to 272 of SEQ ID NO: 34; or

(B) a polypeptide which has an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence comprising at least amino acid residues 22 to 279 of SEQ ID NO: 32, or an amino acid sequence comprising at least amino acid residues 22 to 272 of SEQ ID NO: 34, and which has an activity to support proliferation or survival of hematopoietic stem cell or hematopoietic progenitor cell, with a proviso that C-terminal amino acid sequence does not comprise the amino acid sequence of SEQ ID NO: 46.

10. The DNA according to claim 1, which is:

(a) a DNA which comprises at least nucleotides 574 to 1347 of SEQ ID NO: 31; or

(b) a DNA which is hybridizable with the nucleotide sequence of SEQ ID NO: 31 or a probe prepared from said sequence, under stringent conditions, and which has an activity to support proliferation or survival of hematopoietic stem cell or hematopoietic progenitor cell.

11. The DNA according to claim 10, wherein the stringent conditions are 6 x SSC 5 x Denhardt, 0.5% SDS and 68°C (SSC 3M NaCl, 0.3M sodium citrate, 50 x Denhardt 1% BSA 1% polyvinyl pyrrolidone, 1% Ficoll 400 , or 6 x SSC, 5 x Denhardt, 0.5% SDS, 50% formamide and 42°C.

12. The DNA according to claim 1, which is:

(a) a DNA which comprises at least nucleotides 321 to 1074 of SEQ ID NO: 33; or

(b) a DNA which is hybridizable with the nucleotide sequence of SEQ ID NO: 33 or a prove prepared from said sequence, under stringent conditions, and which has an activity to support proliferation or survival of hematopoietic stem cell or hematopoietic progenitor cell.

13. The DNA according to claim 12, wherein the stringent conditions are 6 x SSC/5 x Denhardt, 0.5% SDS and 68°C (SSC 3M NaCl, 0.3M sodium citrate, 50 x Denhardt/1% BSA/1% polyvinyl pyrrolidone, 1% Ficoll 400, or 6 x SSC, 5 x Deanhardt, 0.5% SDS, 50% Formamide and 42°C.

14. The polynucleotide of any of claims 1, 2 or 3 which is a DNA.

15. An isolated polynucleotide which comprises the complement of the polynucleotide of any one of claims 1, 2 or 3.

16. A vector comprising the polynucleotide of any one of claims 1, 2 or 3

17. An expression vector comprising the polynucleotide any one of claims 1, 2 or 3.

18. A host cell genetically engineered to express the polynucleotide of any one of claims 1, 2 or 3.

19. A host cell genetically engineered to contain the polynucleotide of any one of claims 1, 2 or 3 in operative association with a regulatory sequence that controls expression of the polynucleotide in the host cell.

20. The host cell of claim 19 which has been genetically engineered to contain a heterologous regulatory sequence that increases expression of an endogenous polynucleotide.

21. A method of producing a polypeptide having stem cell growth factor activity comprising growing the host cell of claim 19 in a culture medium under conditions that permit expression of said polypeptide and isolating said polypeptide from said host cell or said culture medium.

22. A polypeptide produced by the method of claim 21.

23. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 10, 13, 16, 32 or 34, or the mature protein portion thereof, or a fragment, analog, variant or derivative thereof that retains stem cell growth factor activity.

24. The polypeptide of claim 23 which is encoded by a polynucleotide of claim 2.

25. The polypeptide of claim 23 which comprises an amino acid sequence having greater than about 85% sequence identity with the nucleotide sequence of SEQ ID NO: 10, 13, 16, 32 or 34.

26. The polypeptide of claim 23 which comprises an amino acid sequence having greater than about 92% sequence identity with the nucleotide sequence of SEQ ID NO: 10, 13, 16, 32 or 34.

27. The polypeptide of claim 23 with the proviso that said polypeptide does not consist of the amino acid sequence of SEQ ID NO: 48.

28. An isolated polypeptide comprising the mature protein portion of SEQ ID NO: 10, 13, 16, 32 or 34.

29. The polypeptide of claim 23, wherein the polypeptide comprises one or more motifs selected from the group of a laminin-type EGF-like domain, a membrane attack complex component/perforin domain, and neurohypophysial hormone signature.

30. A polypeptide which is an expression product of a DNA according to any one of claims 1 through 15, the polypeptide having an activity to support proliferation or survival of hematopoietic stem cell or hematopoietic progenitor cell, with a proviso that C-terminal amino acid sequence does not comprise the amino acid sequence of SEQ ID NO: 46.

31. The polypeptide according to claim 8, which has an amino acid sequence comprising at least amino acid residues 22 to 279 of SEQ ID NO: 32, or an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence comprising at least amino acid residues 22 to 279 of SEQ ID NO: 32

32. The polypeptide according to claim 23, which has an amino acid sequence comprising at least amino acid residues 22 to 272 of SEQ ID NO: 34, or an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence comprising at least amino acid residues 22 to 272 of SEQ ID NO: 34.

33. The polypeptide according to claim 23, which is modified with one or more modifying agent selected from the group consisting of polyethylene glycol (PEG), dextran, poly(N-vinyl-pyrrolidone), polypropylene glycol homopolymer, copolymer of polypropylene oxide/ethylene oxide, polyoxyethylated polyol and polyvinyl alcohol.

34. The polypeptide of claim 23 comprising at least ten consecutive amino acids from SEQ ID NO: 10 or 13.

35. The polypeptide of claim 23, comprising at least ten consecutive amino acids from the C-terminal seventeen amino acids of SEQ ID NO: 10 or 13.

36. A polypeptide with biological activity, said polypeptide comprising at least 272 amino acids and having at least 98% identity with SEQ ID NO: 10.

37. An isolated polypeptide with stem cell growth factor activity having at least 90% identity with SEQ ID NO: 10, 13, or 16 and lacking amino acid sequence GIEVTLAEGLTSVSQRTQPTPCRRRYL (SEQ ID NO: 29) wherein A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine.

38. An isolated polypeptide with stem cell growth factor activity having at least 90% identity with SEQ ID NO: 10, 13, or 16 and lacking any 10 consecutive amino acids from a amino acid sequence GIEVTLAEGLTSVSQRTQPTPCRRRYL (SEQ ID NO: 29), wherein A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine.

39. An isolated polypeptide with stem cell growth factor activity having at least an amino acid sequence SVSVSTVH (SEQ ID NO: 27) or VSVSTVH (SEQ ID NO: 28), wherein A=Alanine, C=Cysteine, D=Aspartic Acid, E= Glutamic Acid, F=Phenylalanine, G=Glycine, H=Histidine, I=Isoleucine, K=Lysine, L=Leucine, M=Methionine, N=Asparagine, P=Proline, Q=Glutamine, R=Arginine, S=Serine, T=Threonine, V=Valine, W=Tryptophan, Y=Tyrosine.

40. A polynucleotide encoding the polypeptide of any one of claims 23 through 39.

41. A kit comprising the polypeptide of claim 23.

42. A culture medium comprising an amount of the polypeptide of claim 23 effective to maintain survival of or promote proliferation of a stem cell or germ cell.

43. A composition comprising the polypeptide of claim 23 and a pharmaceutically acceptable carrier or diluent.

44. The composition of claim 43 that is a pharmaceutical composition.

45. The pharmaceutical composition of claim 44 having an effect to support proliferation or survival of hematopoietic stem cell or hematopoietic progenitor cell, which comprises:

(A) a polypeptide which has an amino acid sequence comprising at least amino acid residues 22 to 279 of SEQ ID NO: 32, or an amino acid sequence comprising at least amino acid residues 22 to 272 of SEQ ID NO: 34; or

(B) a polypeptide which has an amino acid sequence including deletion, substitution or insertion of one or several amino acids in the amino acid sequence comprising at least amino acid residues 22 to 279 of SEQ ID NO: 32, or an amino acid sequence comprising at least amino acid residues 22 to 272 of SEQ ID NO: 34, and which has an activity to support proliferation or survival of hematopoietic stem cell or hematopoietic progenitor cell.

46. An antibody that binds to the polypeptide of claim 23.

47. The antibody of claim 19 that specifically binds to a polypeptide having the amino acid sequence of SEQ ID NO: 10, 13, 16, 32 or 34.

48. The antibody of claim 20 that does not bind to a polypeptide having the amino acid sequence of SEQ ID NO: 48.

49. The antibody of claim 19 that is a polyclonal antibody, monoclonal antibody, antibody fragment, chimeric antibody, or humanized antibody.

50. A kit comprising the antibody of claim 17.

51. A method for detecting the polynucleotide of claim 1 in a sample, comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex; and

b) detecting the complex, so that if a complex is detected, the polynucleotide is detected.

52. A method for detecting the polynucleotide of claim 1 in a sample, comprising:

a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to the polynucleotide under such conditions;

b) amplifying a product comprising at least a portion of the polynucleotide; and

c) detecting said product and thereby the polynucleotide in the sample.

53. The method of claim 52, wherein the polynucleotide is an RNA molecule that encodes a polypeptide of claim 23, and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.

54. A method for detecting the polypeptide of claim 23 in a sample, comprising:

a) contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex; and

b) detecting formation of the complex, so that if a complex formation is detected, the polypeptide is detected.

55. A method for identifying a compound that binds to the polypeptide of claim 23, comprising:

a) contacting the compound with the polypeptide under conditions and for a time sufficient to form a polypeptide/compound complex; and

b) detecting the complex, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide is identified.

56. A method for identifying a compound that binds to the polypeptide of claim 23, comprising:

a) contacting the compound with the polypeptide, in a cell, for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and

b) detecting the complex by detecting reporter gene sequence expression, so that if the polypeptide/compound complex is detected, a compound that binds to the polypeptide is identified.

57. A nucleic acid array comprising the polynucleotide of claim 1 or a unique segment of the polynucleotide of claim 1 attached to a surface.

58. The array of claim 57, wherein the array detects full-matches to the polynucleotide or a unique segment of the polynucleotide of claim 1.

59. The array of claim 57, wherein the array detects mismatches to the polynucleotide or a unique segment of the polynucleotide of claim 1.

60. A method of treatment of a subject in need of enhanced activity or expression of stem cell growth factor-like polypeptide of claim 23 comprising administering to the subject:

(a) a composition comprising a therapeutic amount of an agonist of said polypeptide;

(b) a composition comprising a therapeutic amount of the polypeptide; or

(c) a composition comprising a therapeutic amount of a polynucleotide encoding the polypeptide in form and under conditions such that the polypeptide is produced;

said composition comprising a pharmaceutically acceptable carrier or diluent.

61. A method of treatment of a subject having need of decreased activity or expression of stem cell growth factor-like polypeptide of claim 23 comprising administering to the subject:

(a) a composition comprising a therapeutic amount of an antagonist of said polypeptide;

(b) a composition comprising a therapeutic amount of the polynucleotide that inhibits the expression of the nucleotide sequence encoding said polypeptide; and

(c) a composition comprising a therapeutic amount of a polypeptide that competes with the stem cell growth factor-like polypeptide for its ligand;

said composition comprising a pharmaceutically acceptable carrier or diluent.

62. A method of supporting proliferation or survival of a stem cell or germ cell comprising contacting said cell with an amount of a polypeptide of claim 23 effective to maintain survival of or promote proliferation of said cell.

63. The method of claim 62 wherein said cell is a primordial germ cell, germ line stem cell, embryonic stem cell, hematopoietic stem cell, hematopoietic progenitor cell, pluripotent cell, or totipotent cell.

64. The method of claim 62, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 10, 13, or 16, or comprises an amino acid sequence 90% identical to SEQ ID NO: 10, 13, or 16.

65. The method of claim 62, wherein the stem cell growth factor-like polypeptide is encoded by a polynucleotide that hybridizes to the complement of a polynucleotide encoding SEQ ID NO: 10, 13, or 16 under stringent hybridization conditions.

66. A stromal cell genetically engineered to express a polypeptide of claim 23 in an amount effective to support proliferation or survival of a stem cell or germ cell.

67. The stromal cell of claim 66 wherein said cell is a primordial germ cell, germ line stem cell, embryonic stem cell, hematopoietic stem cell, hematopoietic progenitor cell, pluripotent cell, or totipotent cell.

68. An implant comprising a cell genetically engineered to express a polypeptide of claim 23 in an amount effective to support proliferation or survival of a stem cell or germ cell.

69. The implant of claim 68 wherein said cell is a primordial germ cell, germ line stem cell, embryonic stem cell, hematopoietic stem cell, hematopoietic progenitor cell, pluripotent cell, or totipotent cell.

70. An isolated polynucleotide comprising the protein coding cDNA insert of the plasmid deposited with the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology (Zip code 305-8566; Higashi 1-1-3, Tsukuba, Ibaraki, Japan) on June 26,2000 under accession number FERM BP-7198.

72. The mature polypeptide expressed by the polynucleotide of claim 70 in a suitable host cell.

73. An isolated polynucleotide comprising the protein coding cDNA insert of the plasmid deposited with the National Institute of Bioscience and Human-Technology, Agency of Industrial Science and Technology (Zip code 305-8566; Higashi 1-1-3, Tsukuba, Ibaraki, Japan) on June 26,2000 under accession number FERM BP-7197.

74. The mature polypeptide expression product expressed by the polynucleotide of claim 73 in a suitable host cell.